

Synchrotron Medical Research Applications

Dean Chapman

Anatomy and Cell Biology

University of Saskatchewan

NSLS-II Workshop

Imaging - Nanoprobe

Breakout Session

15 March 2004

Brookhaven National Laboratory



*Canadian Centre canadien
Light de rayonnement
Source synchrotron*



Flower icon Imaging based on interactions:

- Flower icon Absorption imaging
 - Flower icon Dual Energy Imaging
 - Flower icon Computed Tomography
- Flower icon Refraction and scatter imaging
 - Flower icon Phase Contrast
 - Flower icon Diffraction Enhanced Imaging / Multiple Image Radiography

Flower icon Radiotherapy

- Flower icon CT Radiotherapy
- Flower icon Microbeam Radiation Therapy

Flower icon Requirements & Conclusion



Medical Research Opportunities

COMPUTED
TOMOGRAPHY

RADIATION
THERAPY

MAMMOGRAPHY

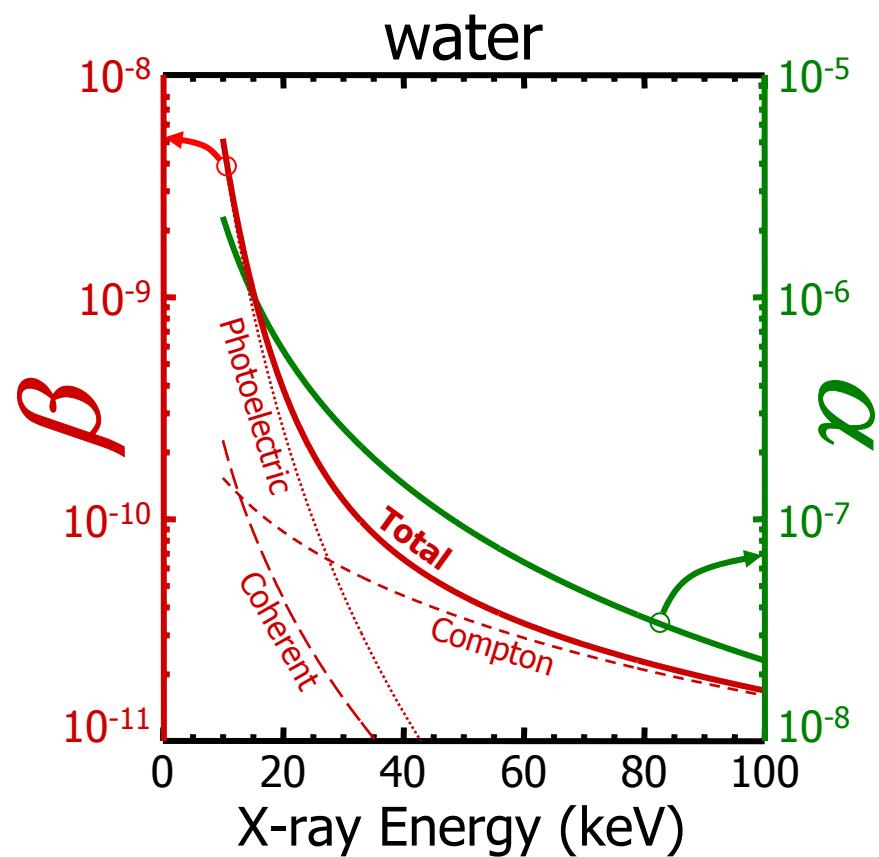
CORONARY
ANGIOGRAPHY

CARTILAGE

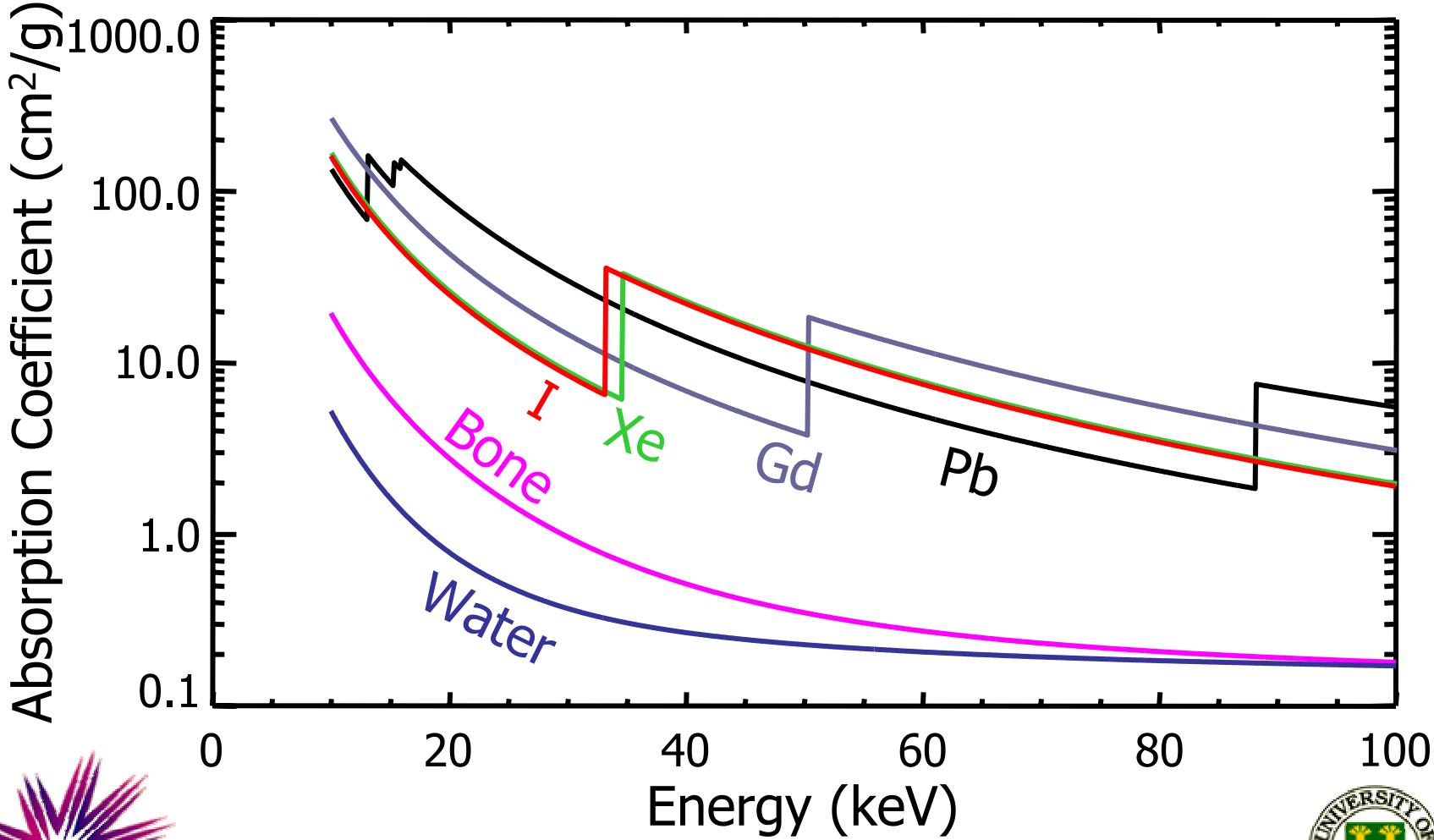


Interaction of X-rays with Matter

- Optical Effects – index of refraction
 - In the x-ray energy range
 - $n = 1 - \alpha - i\beta$
 - Refractive index correction is weak; $\alpha & \beta \ll 1$
 - Absorption index is weaker; $\beta \ll \alpha$

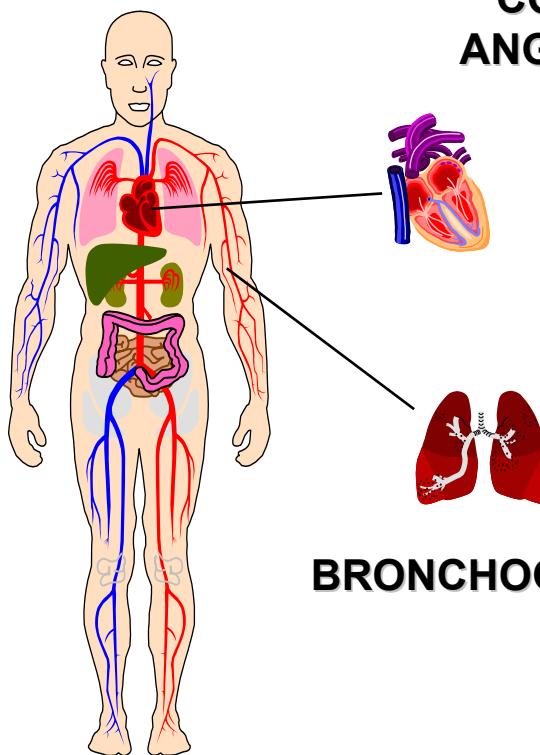


Absorption of Some Materials



Cardiopulmonary Research

**CORONARY
ANGIOGRAPHY**

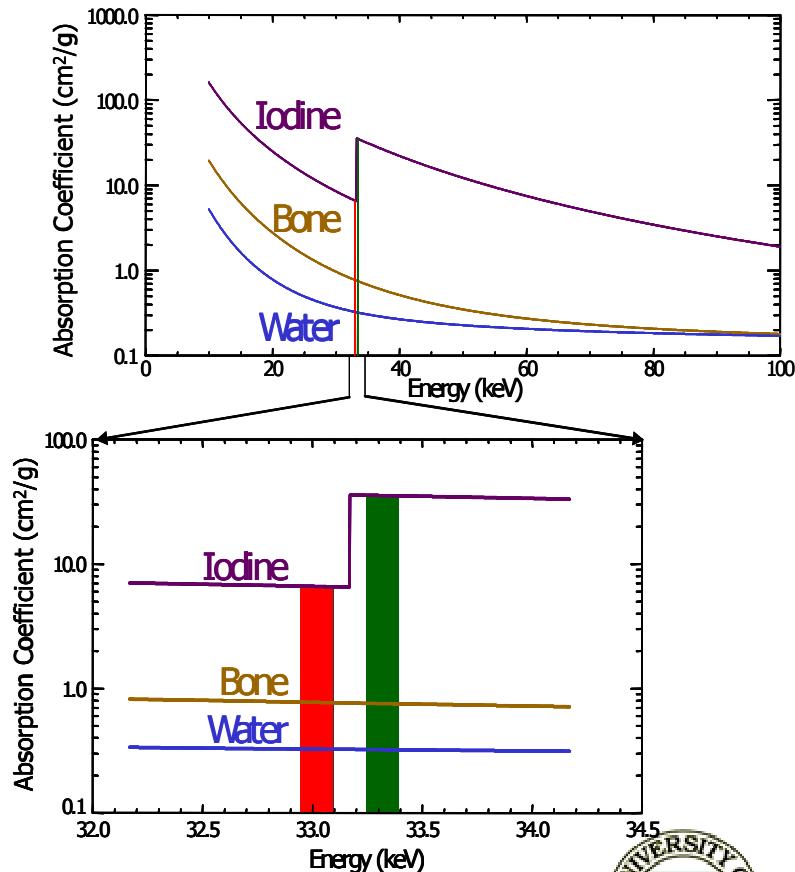


BRONCHOGRAPHY

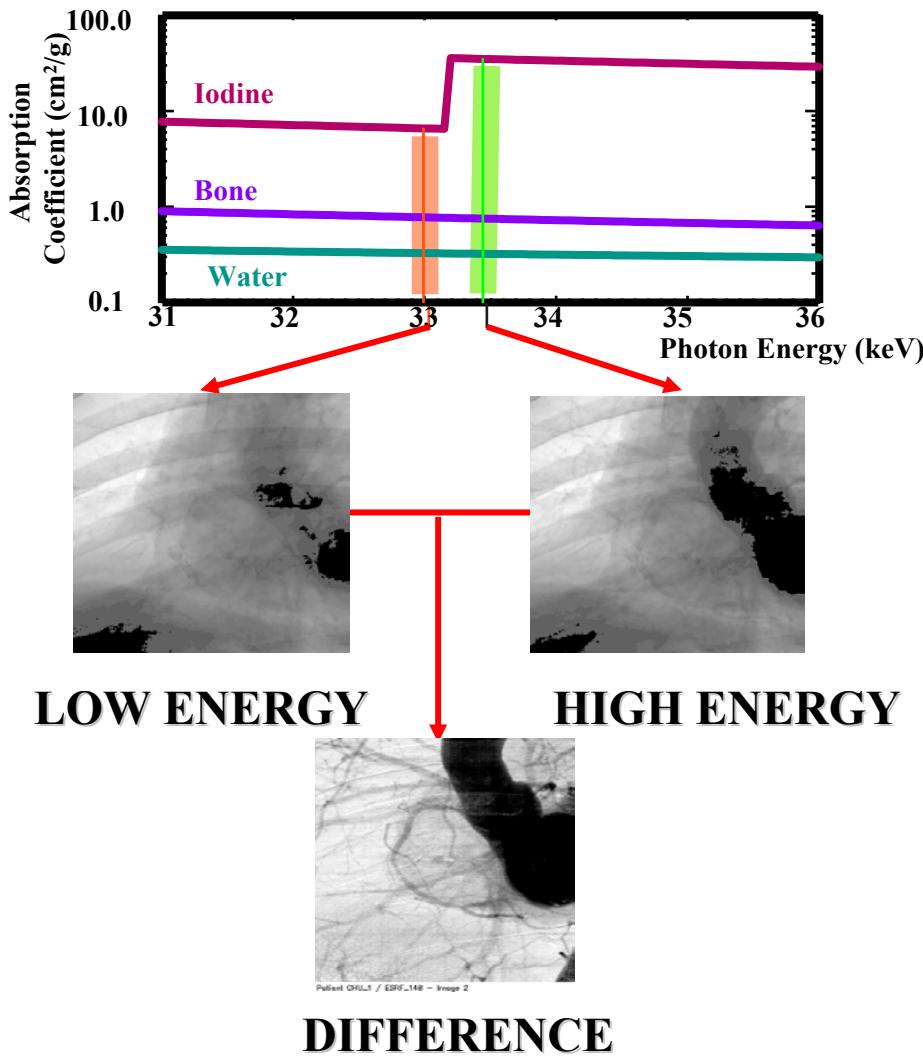


Iodine Absorption- Dual Energy Subtraction

- ✿ Dual energy subtraction makes use of rapid change in absorption of a contrast agent near its absorption edge
 - ✿ If images are taken near this edge, absorption of other materials in the object change very little
 - ✿ Object can be thought of as a two component system...contrast agent and rest of object
 - ✿ => take two images on each side of edge; solve for the two components



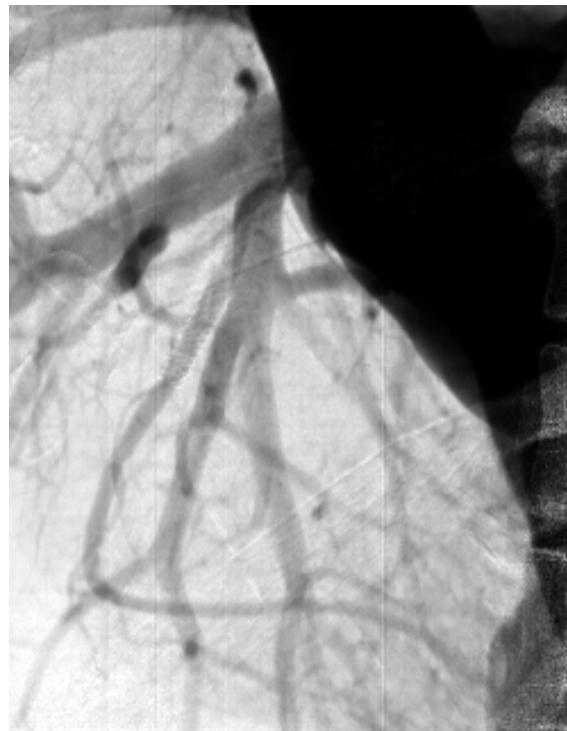
Dual Energy Subtraction Imaging- Iodine Contrast Imaging – Coronary Angiography



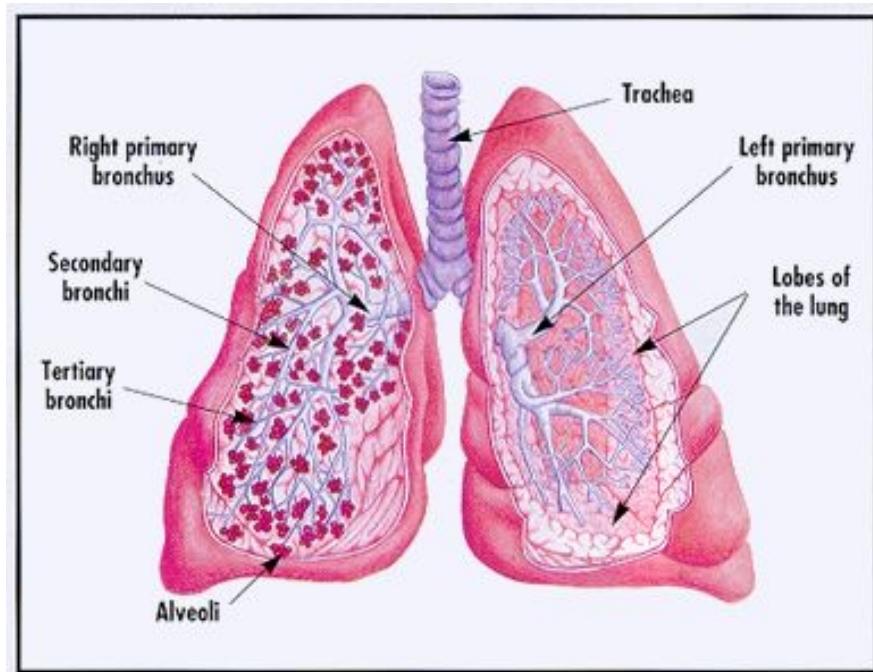
Courtesy W. Thomlinson & M. Renier



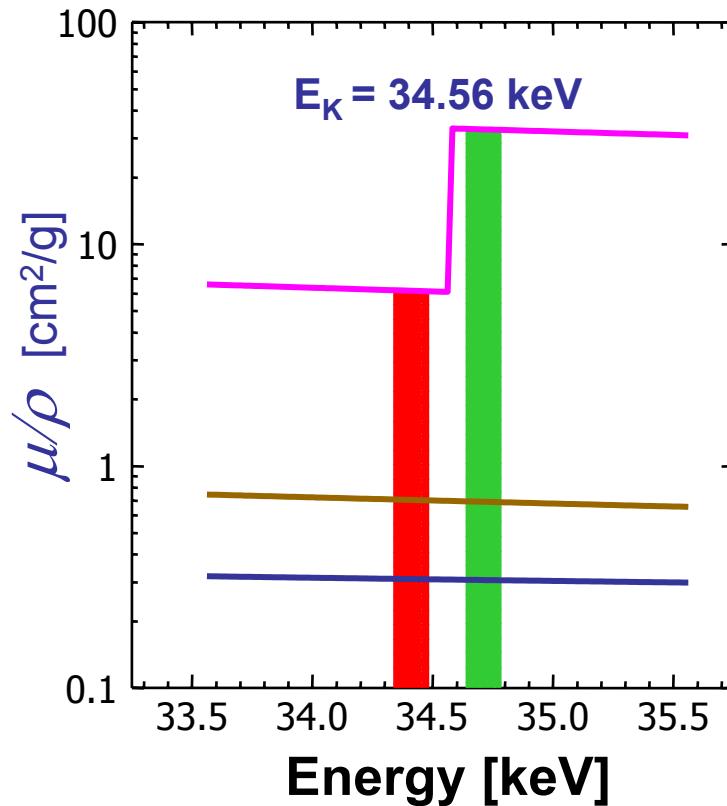
Best Views- ID17 Imaging Facility ESRF



Xe K-edge Imaging of Lungs



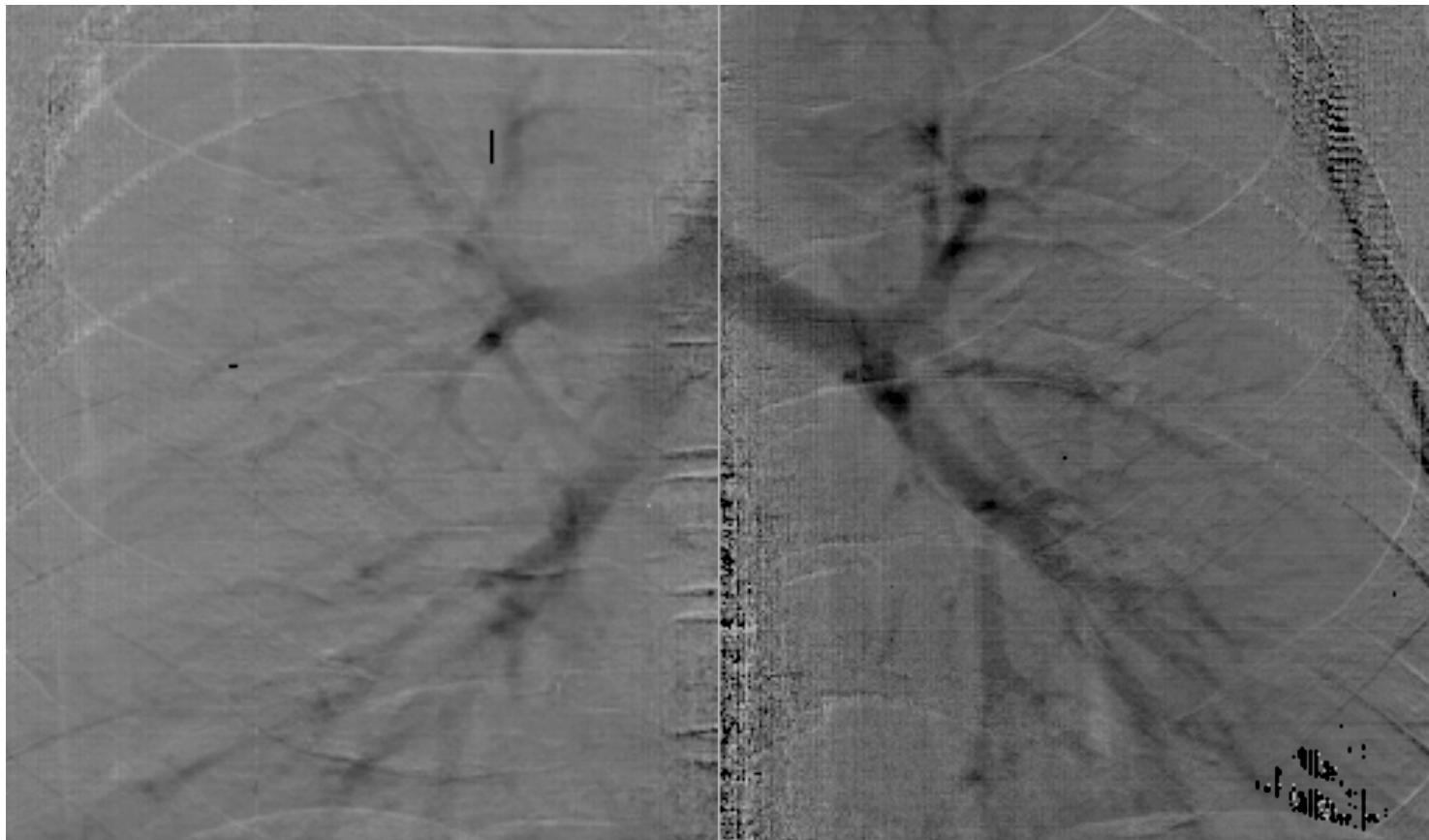
Attenuation Coefficient of Xe



Human Bronchography

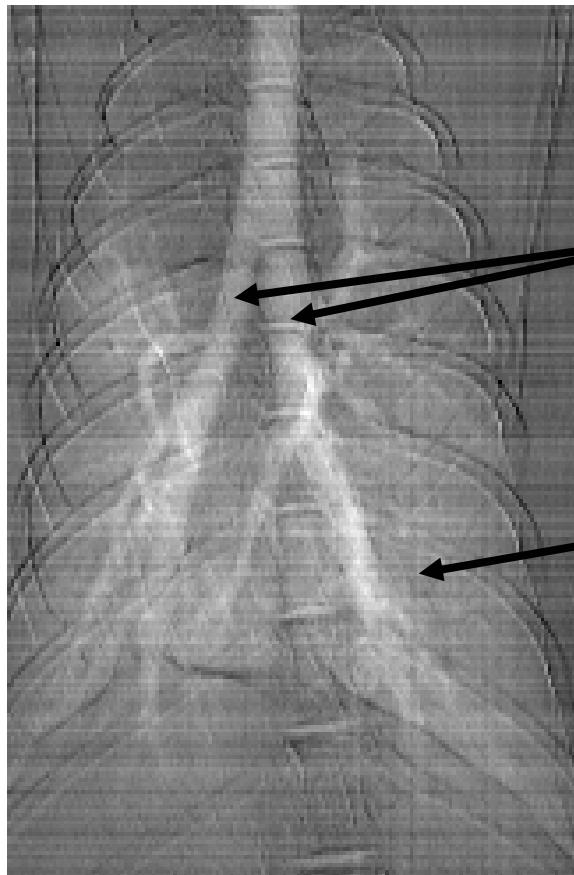
The Sample

Giacomini, Rubenstein Gordon, O'Neil, Van Kessel, Cason, Chapman, Lavender, Gmür, Menk, Thomlinson, Zhong



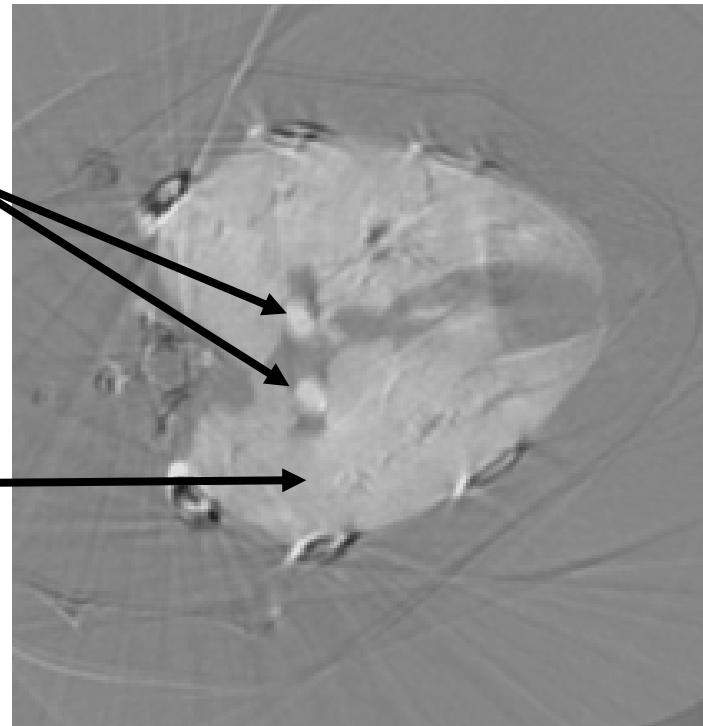
NSLS X17B2, 1996; NIM A406:473-478 (1998)

Bronchography In-Vivo Rabbit Xenon K-Edge Imaging



Bronchi

Alvioli



Computed Tomography
Image

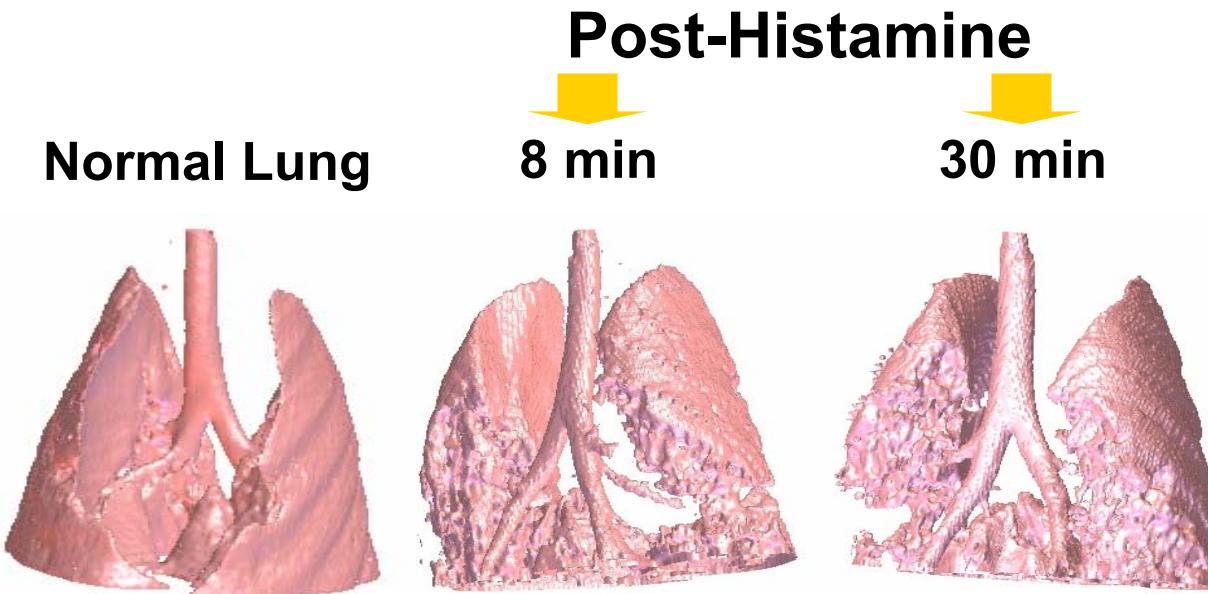
Courtesy W. Thomlinson & M. Renier
NSLS-II Workshop / Imaging - Nanoprobe 15 Mar 2004 Brookhaven National Laboratory



Projection Image

Cardiopulmonary Physiology and Perfusion Studies

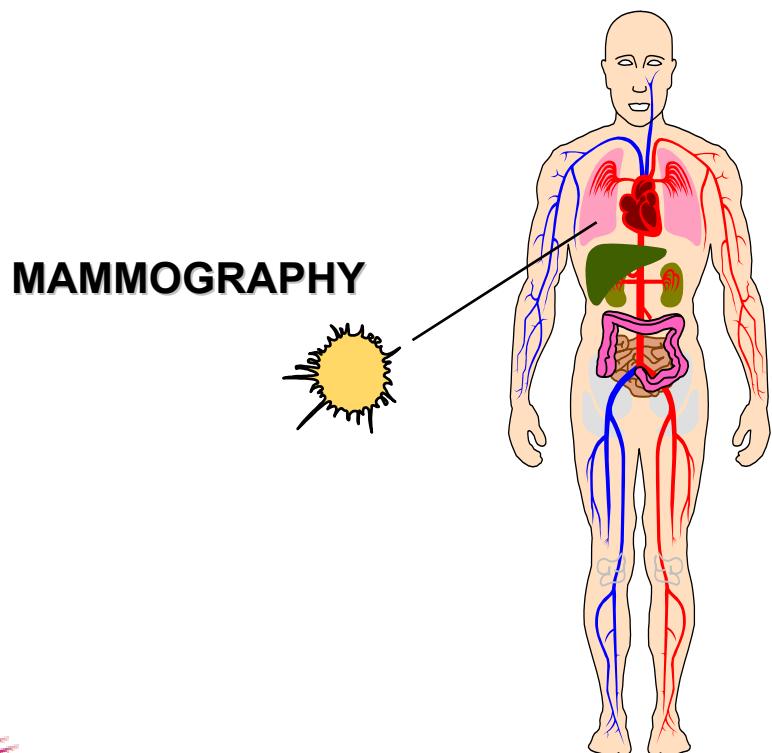
✖ Xe perfusion studies of rabbit model system under influence of histamine



Spiral CT Xe KES



Mammography

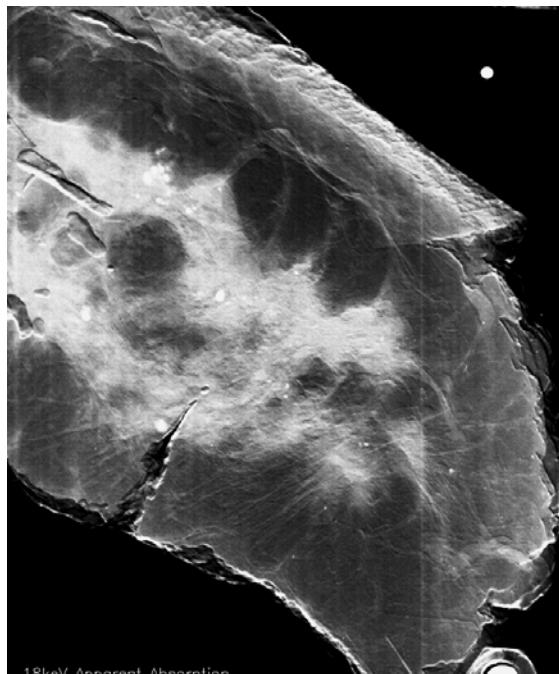


Cancer in Breast Tissue

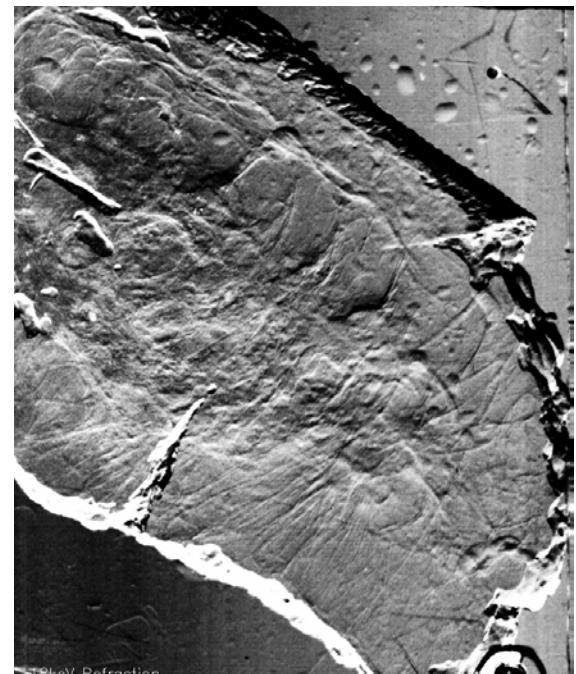
Pisano, Johnston(UNC); Sayers(NCSU); Zhong(BNL);
Thomlinson(ESRF); Chapman(IIT)



Conventional

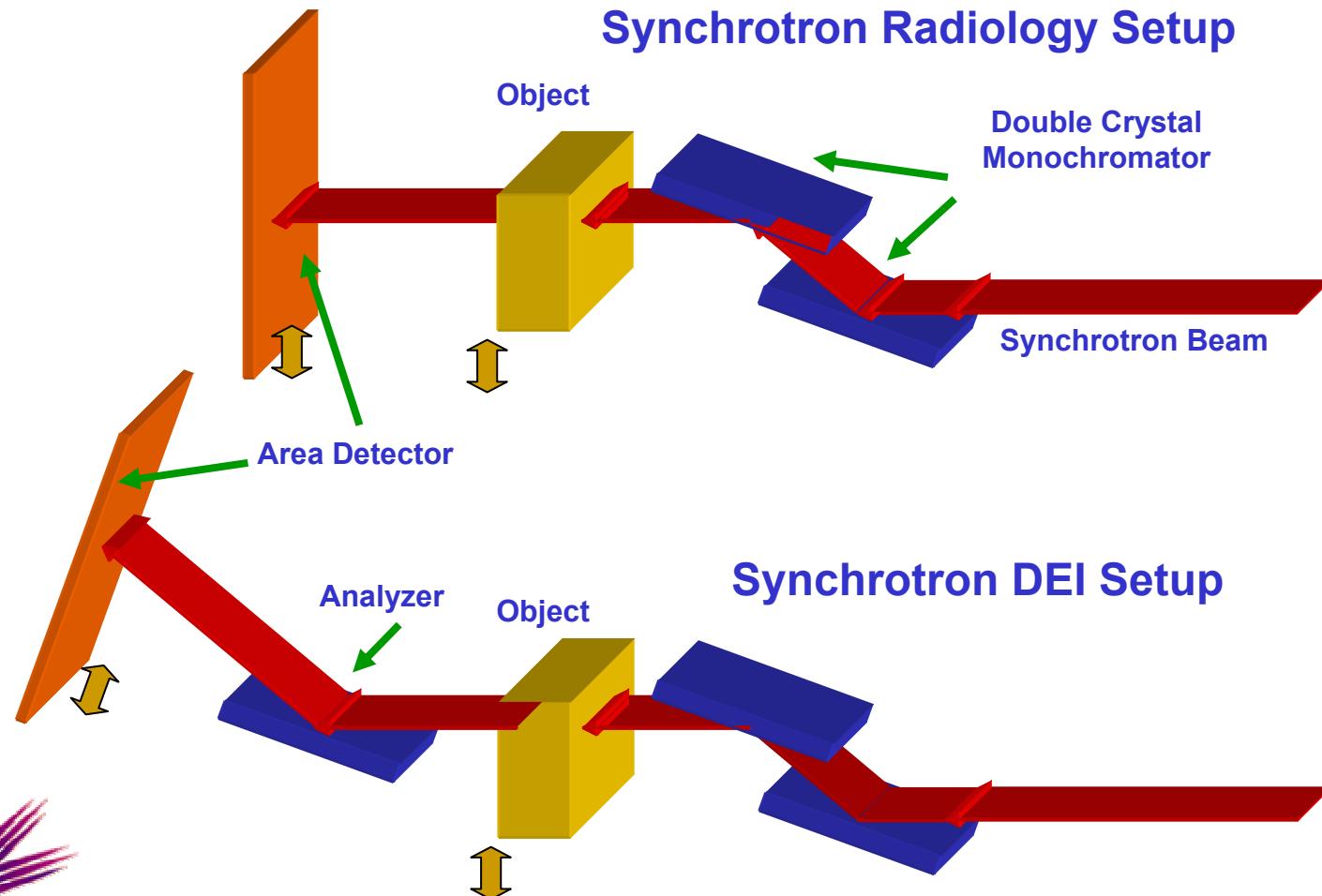


DEI - Absorption



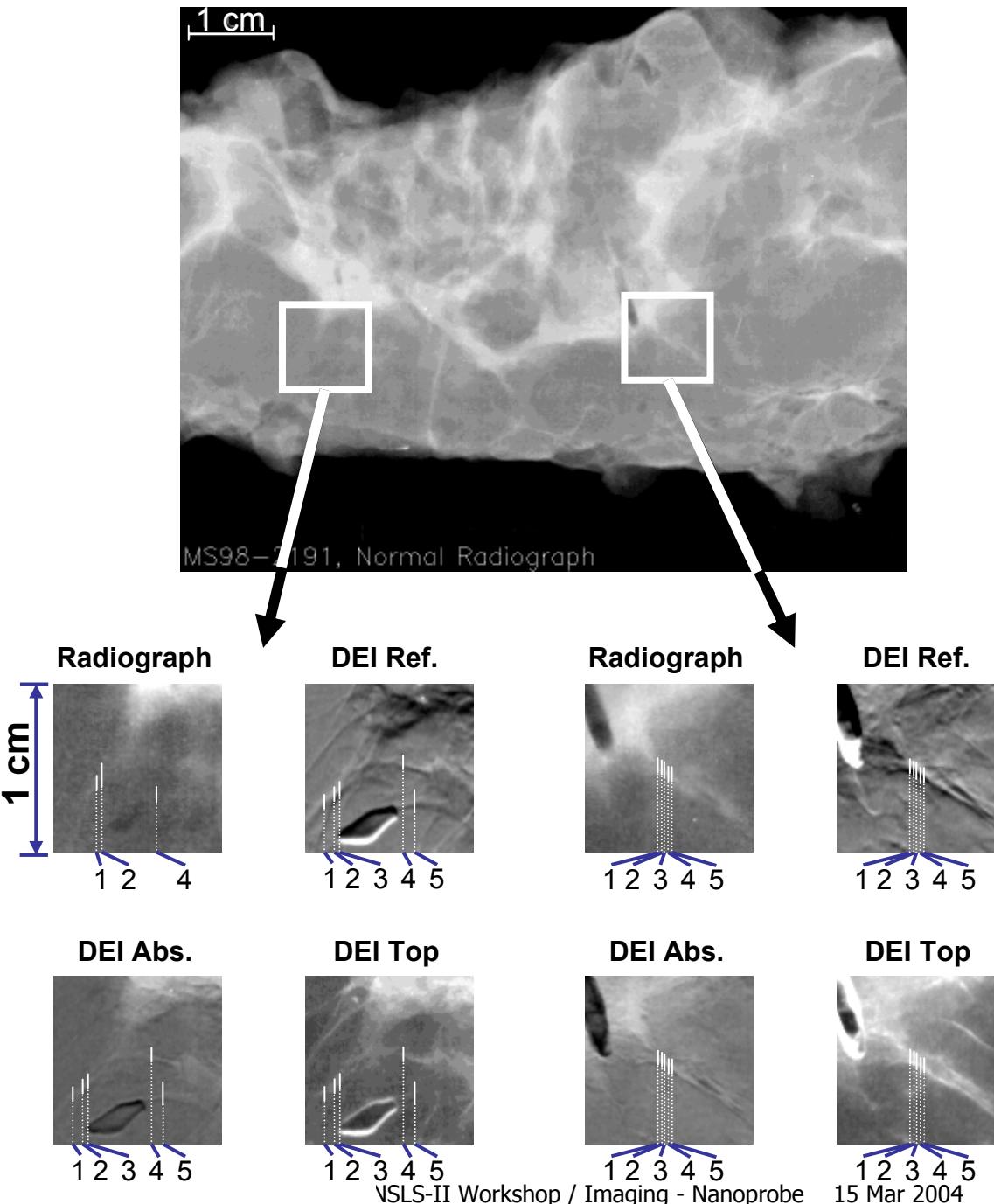
DEI - Refraction

Synchrotron Radiography and DEI



Invasive Lobular Carcinoma Analysis

Hasnah, Oltulu, Chapman(IIT), Pisano (UNC); Zhong(BNL)



Compared

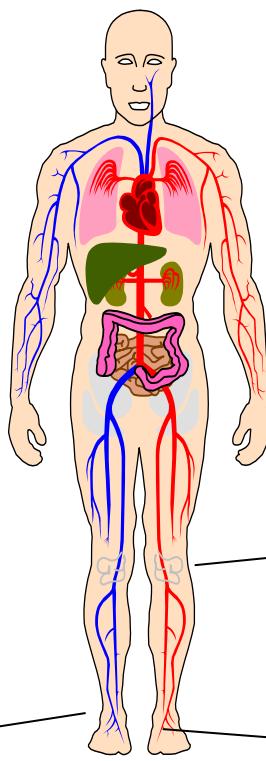
- Radiograph
- DEI Ref. Angle
- DEI App. Abs.
- DEI Top

Found that:

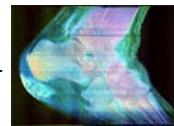
- Absorption \Leftrightarrow refraction
- DEI Absorption contrast compared to radiograph was:
 - $\sim 8 - 14 \times$ higher
- DEI TOP Image has
 - $\sim 12 - 33 \times$ higher



Musculoskeletal Research



CARTILAGE



Mouse Images

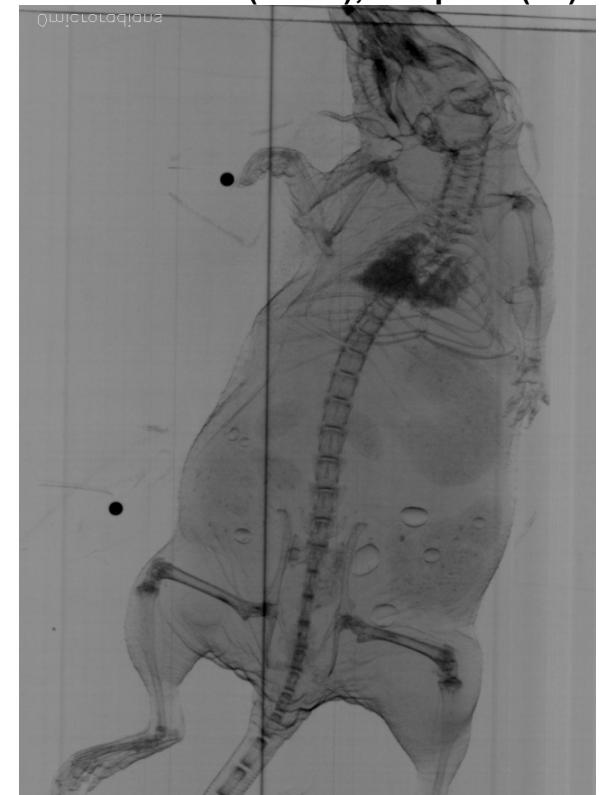
Pisano, Johnston(UNC); Sayers(NCSU); Zhong(BNL);
Thomlinson(ESRF); Chapman(IIT)



18keV



30keV



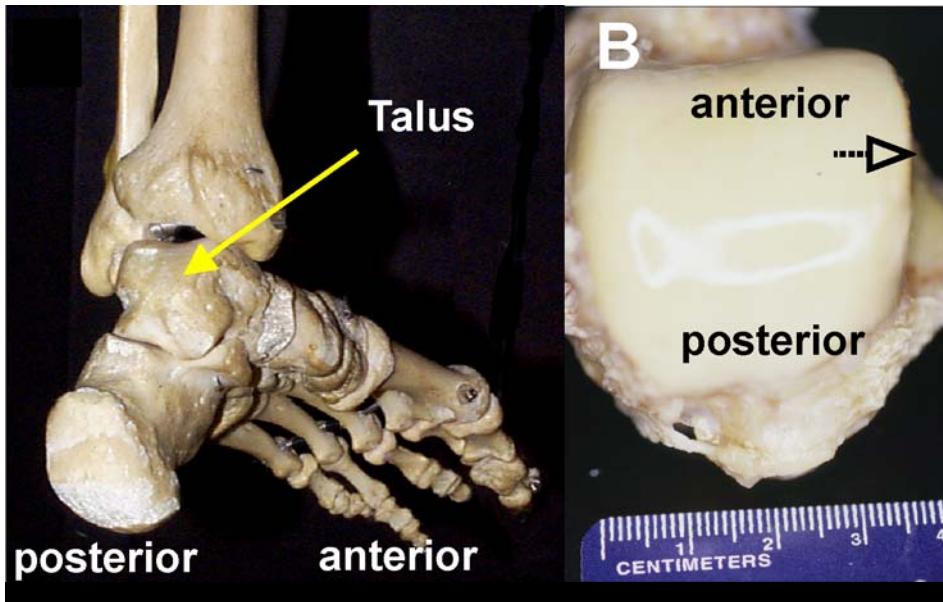
DEI 30keV



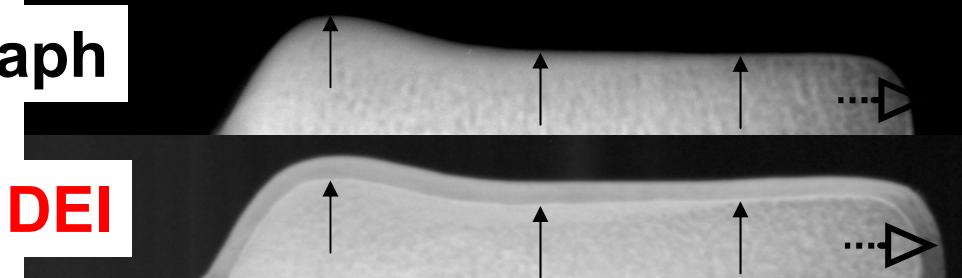
Human Cartilage Imaging

Ankle Joint - Talus

Aurich, Mollenhauer, Cole, Muehleman, Kuettner(Rush);
Zhong(BNL); Hasnah, Oltulu, Chapman(IIT)



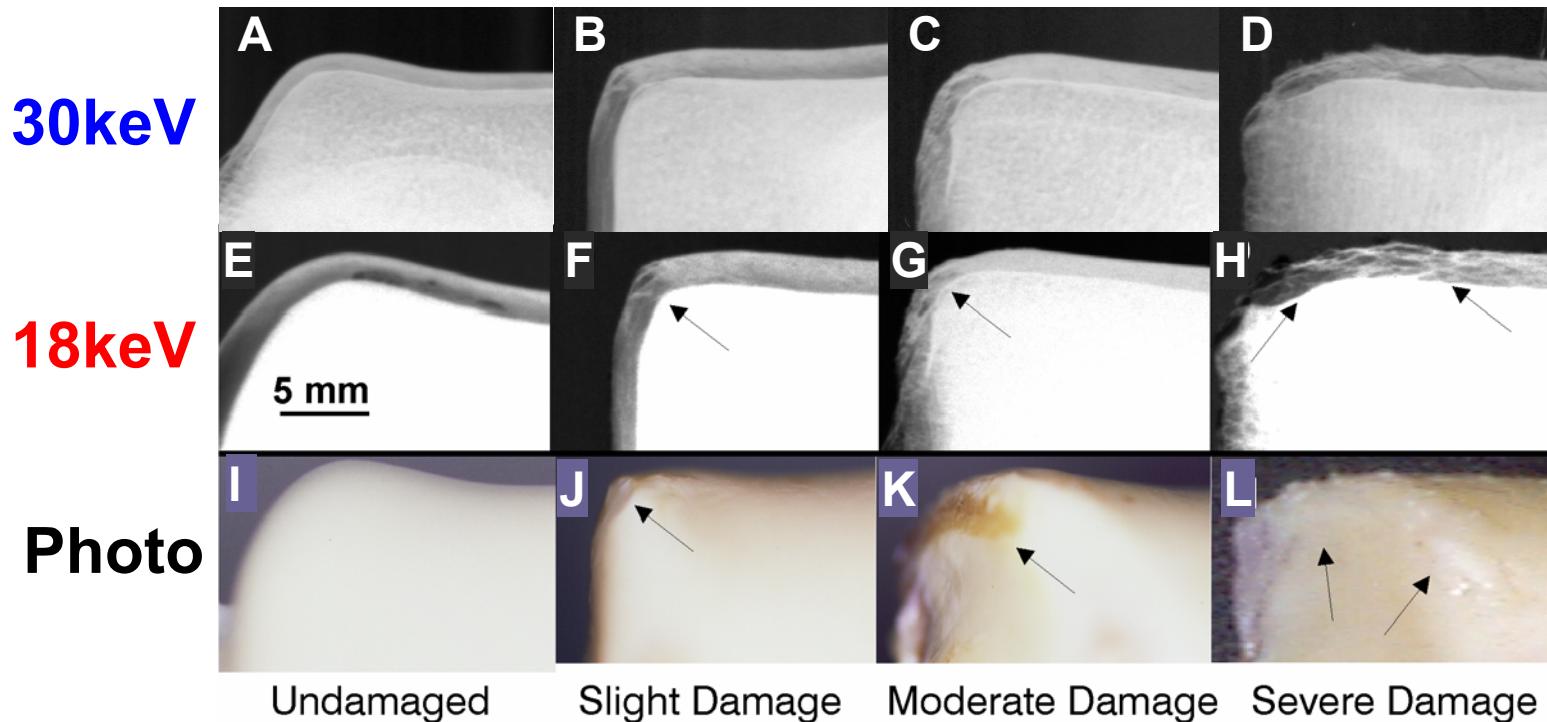
Radiograph



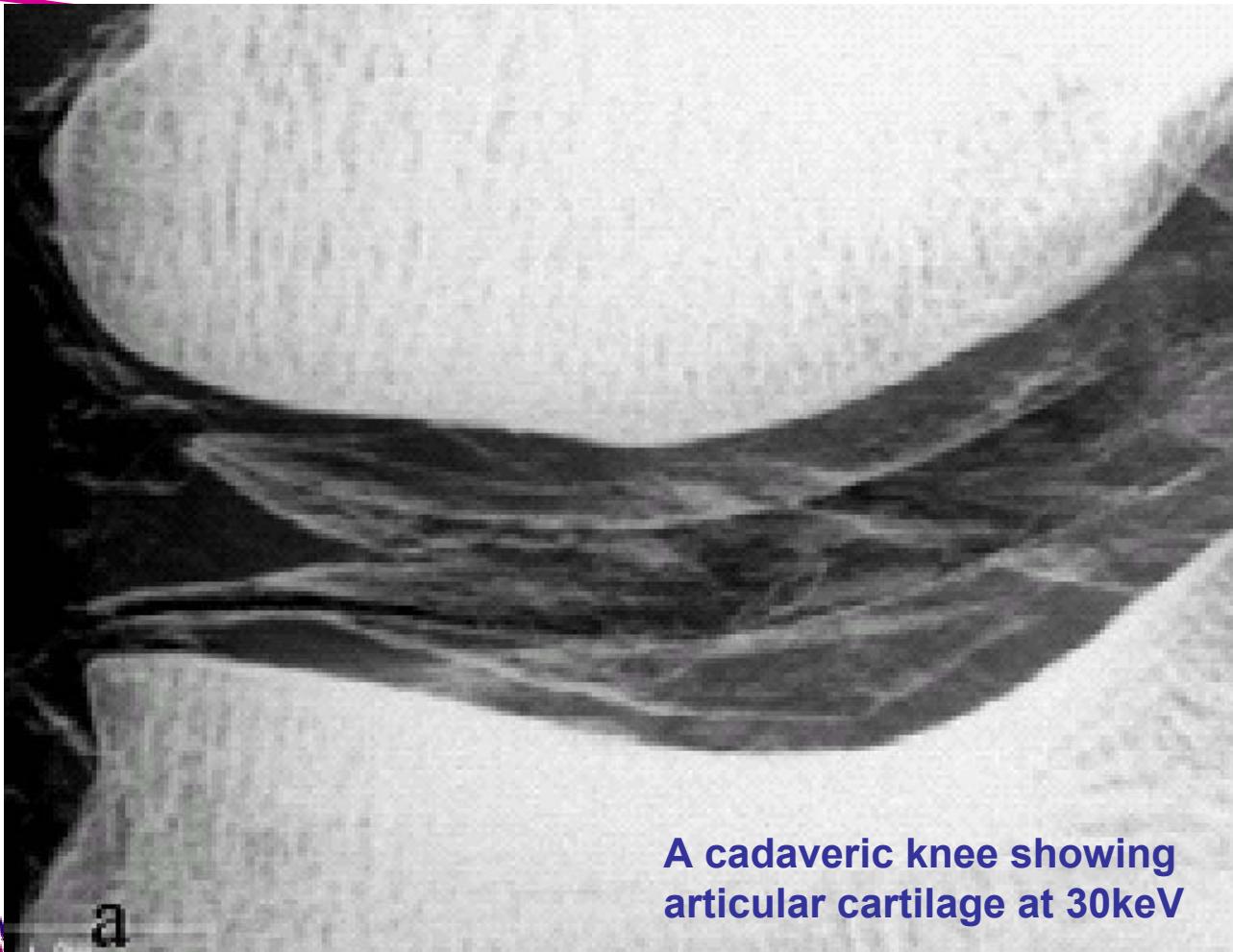
Human Cartilage Imaging

Ankle Joint - Talus

Aurich, Mollenhauer, Cole, Muehleman, Kuettner(Rush);
Zhong(BNL); Hasnah, Oltulu, Chapman(IIT)



Human Cartilage Imaging – Intact Knee Joint

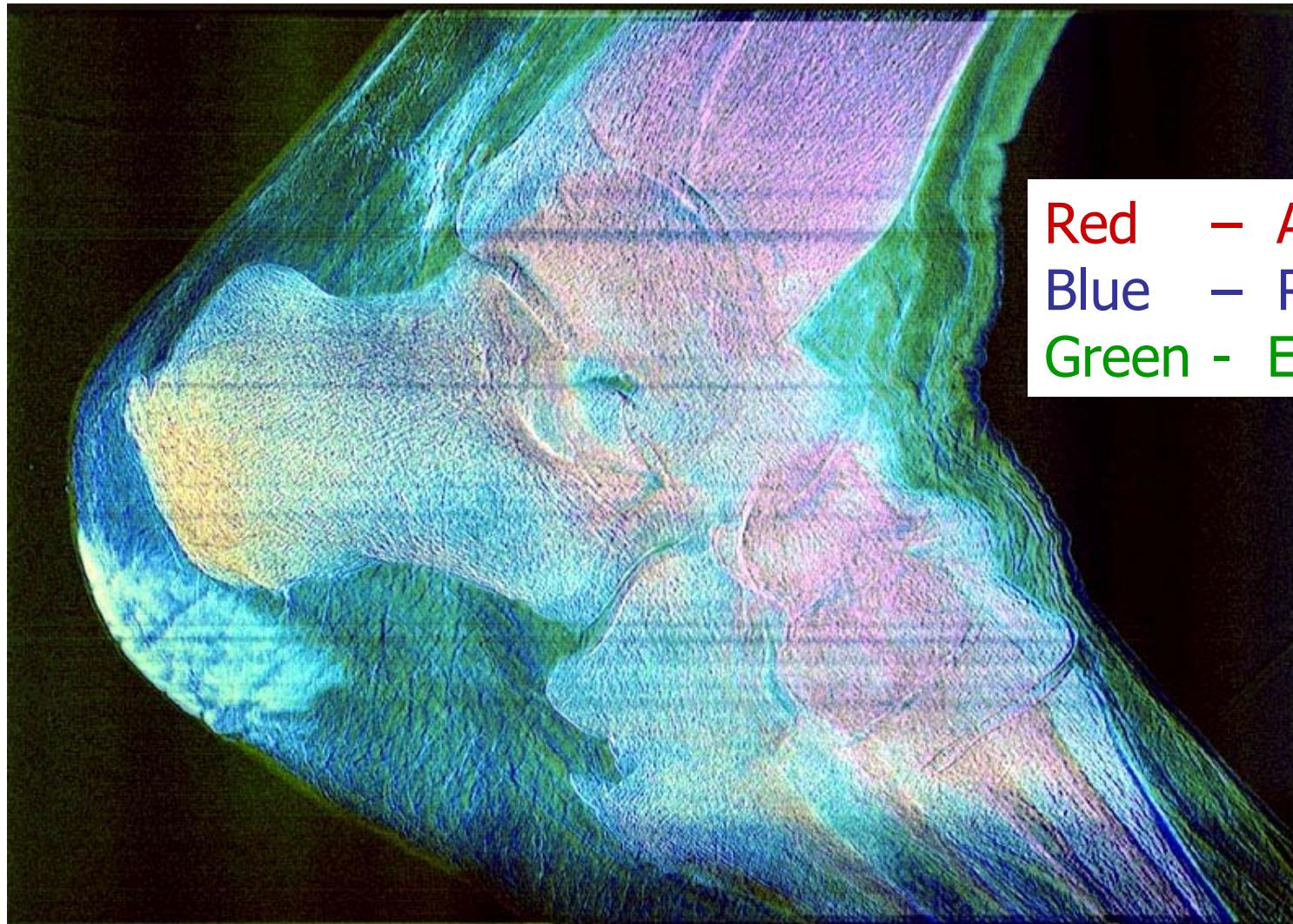


A cadaveric knee showing
articular cartilage at 30keV



Multiple Image Radiography- projection image of a foot

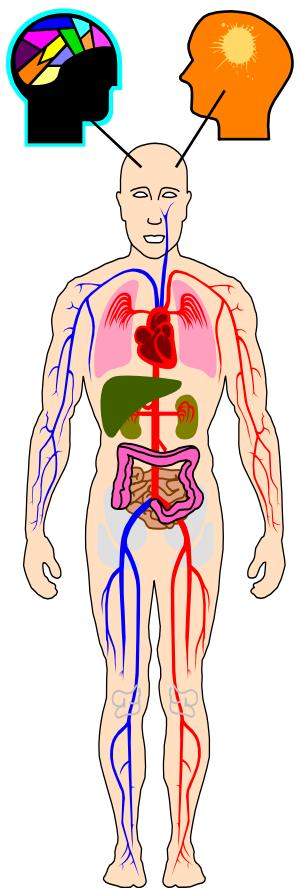
Muehleman, Jun (Rush), Brankov, Wernick, Chapman(IIT);
Zhong(BNL)



Radiation Therapy

COMPUTED
TOMOGRAPHY

RADIATION
THERAPY



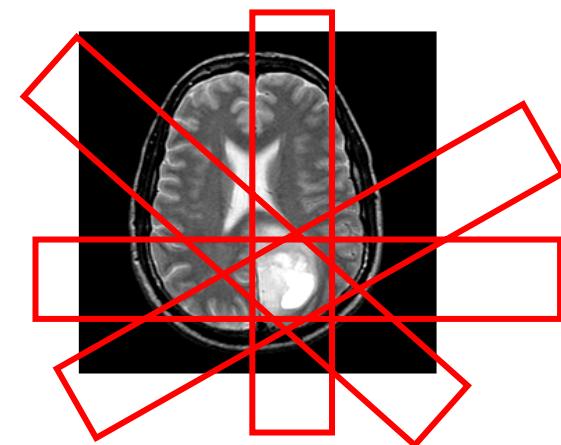
CT-Therapy

History:

- 1980 Mello, Norman, Solberg, Iwamoto
'Radiation dose enhancement with iodine'
- 1999: first ct-therapy with patients

Principle:

- Tumor loaded with a contrast agent
(Iodine or gadolinium).
- Beam size adjusted to the tumor dimensions
- Irradiation with **monochromatic** x-ray beam.
- Tumor positioned at the center of rotation.



Courtesy W. Thomlinson & M. Renier

CT-Therapy Principle

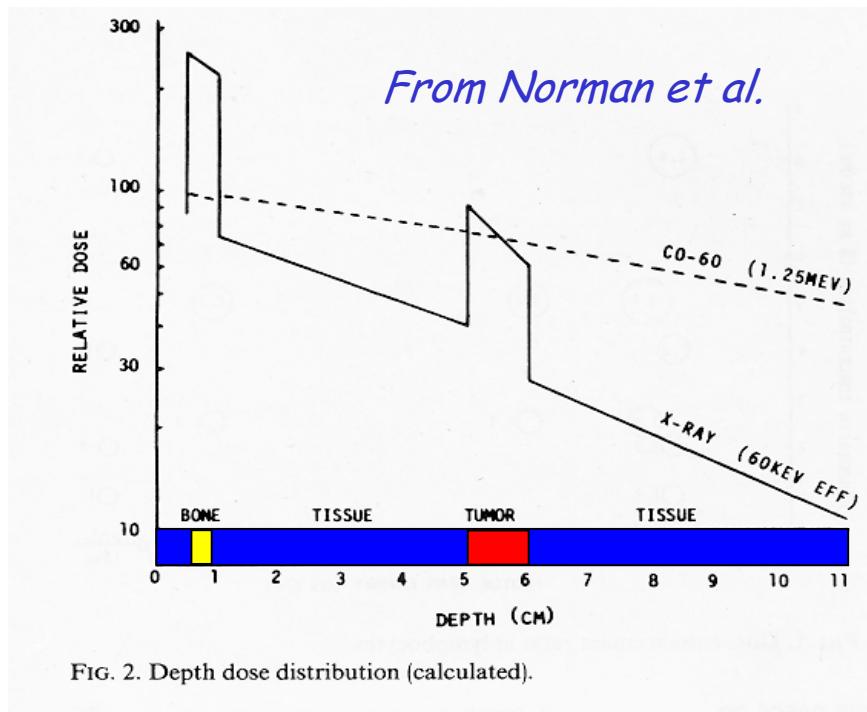
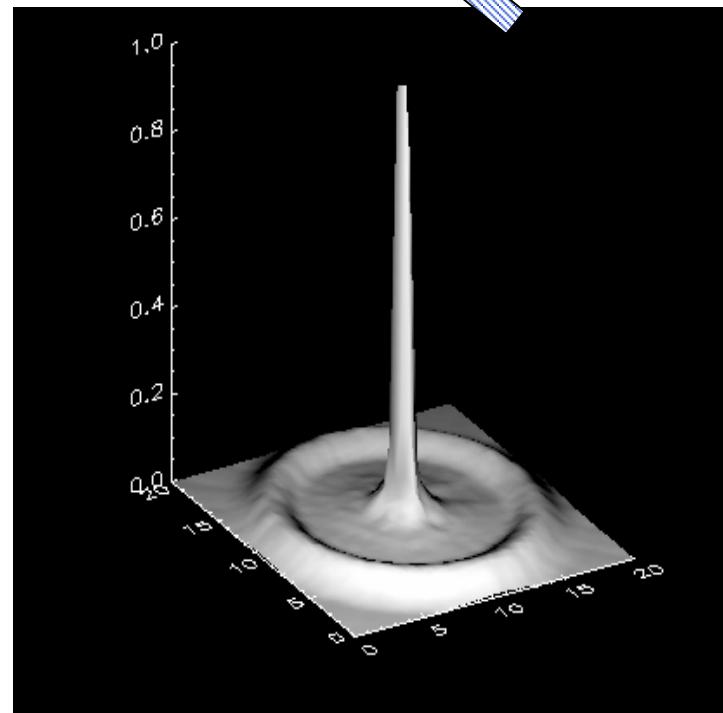
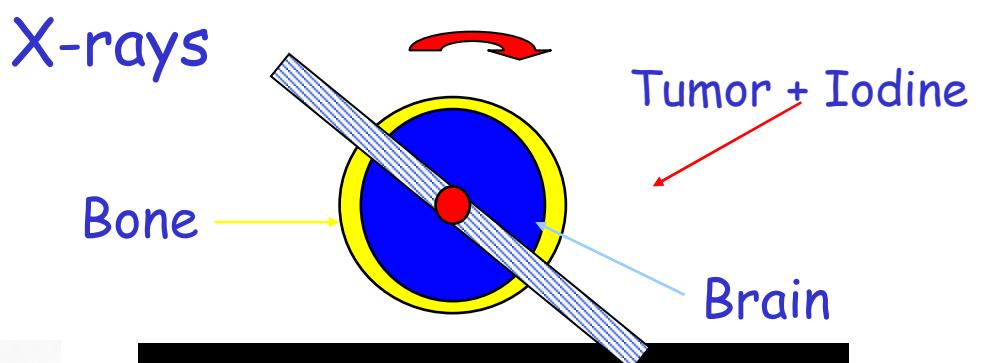


FIG. 2. Depth dose distribution (calculated).

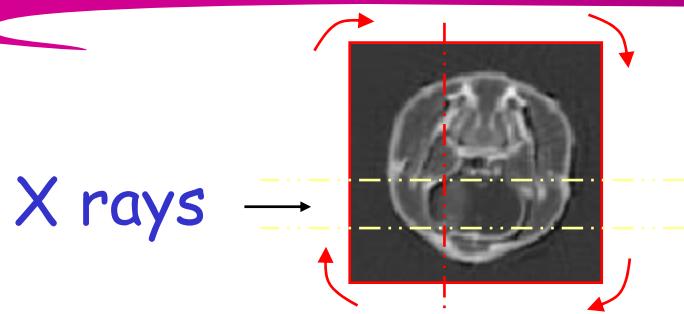


Dose enhancement effect; Beam crossing
at the tumor & Iodine enhancement

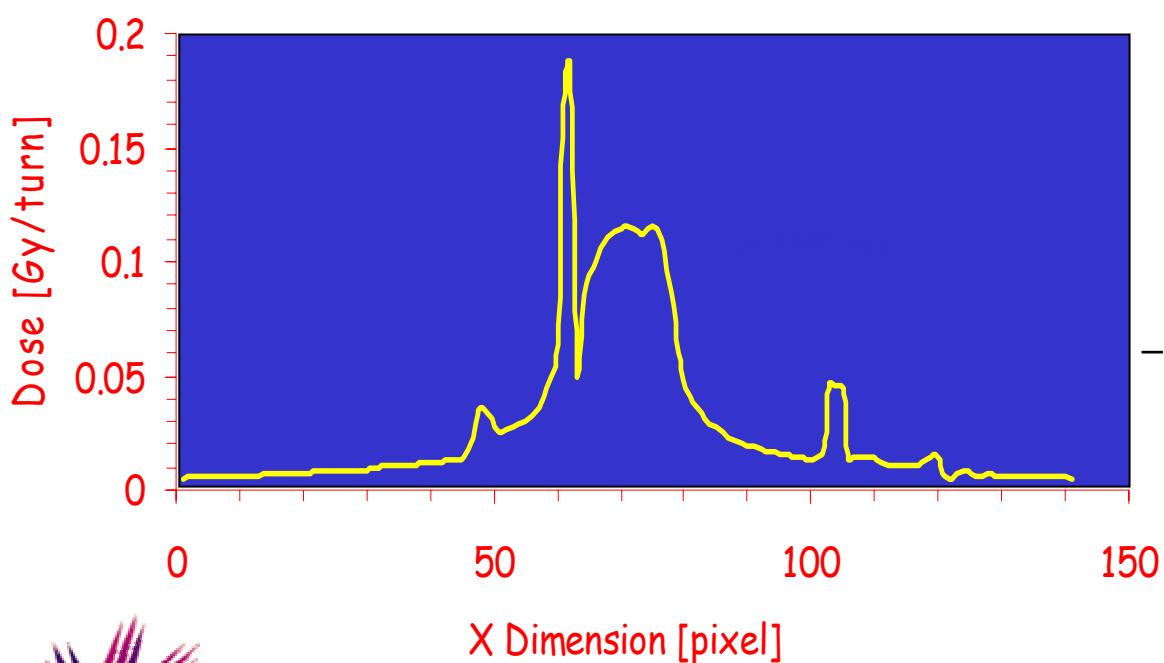


Courtesy W. Thomlinson & M. Renier

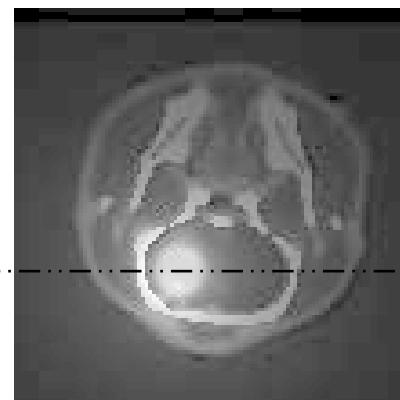
CT-Therapy



- $c_I: 2.5 \text{ mg/ml}$
- Irradiation time: 60 mn



Dose Image



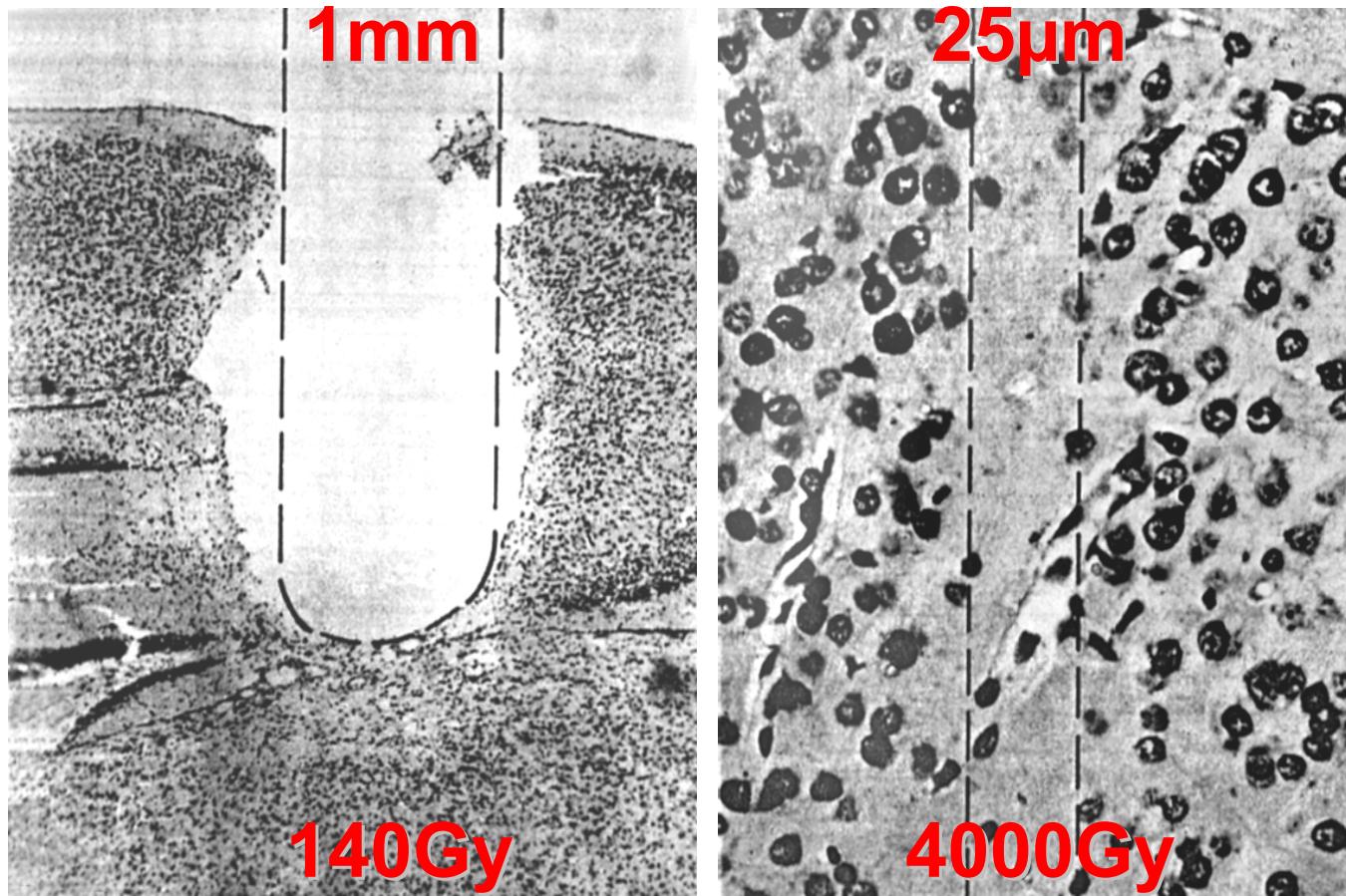
Microbeam Radiation Therapy

- ❖ Has tissue sparing effect due to small dimension of x-ray beam
- ❖ Requires high dose to small area => true synchrotron application
- ❖ Uses filtered high x-ray energy spectrum

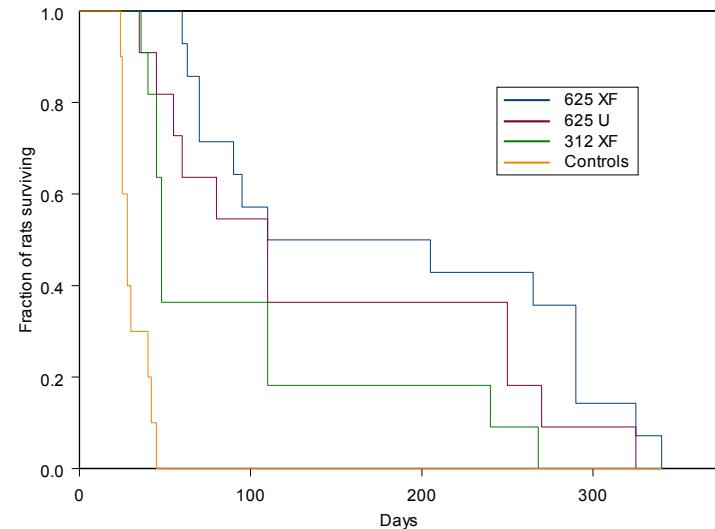
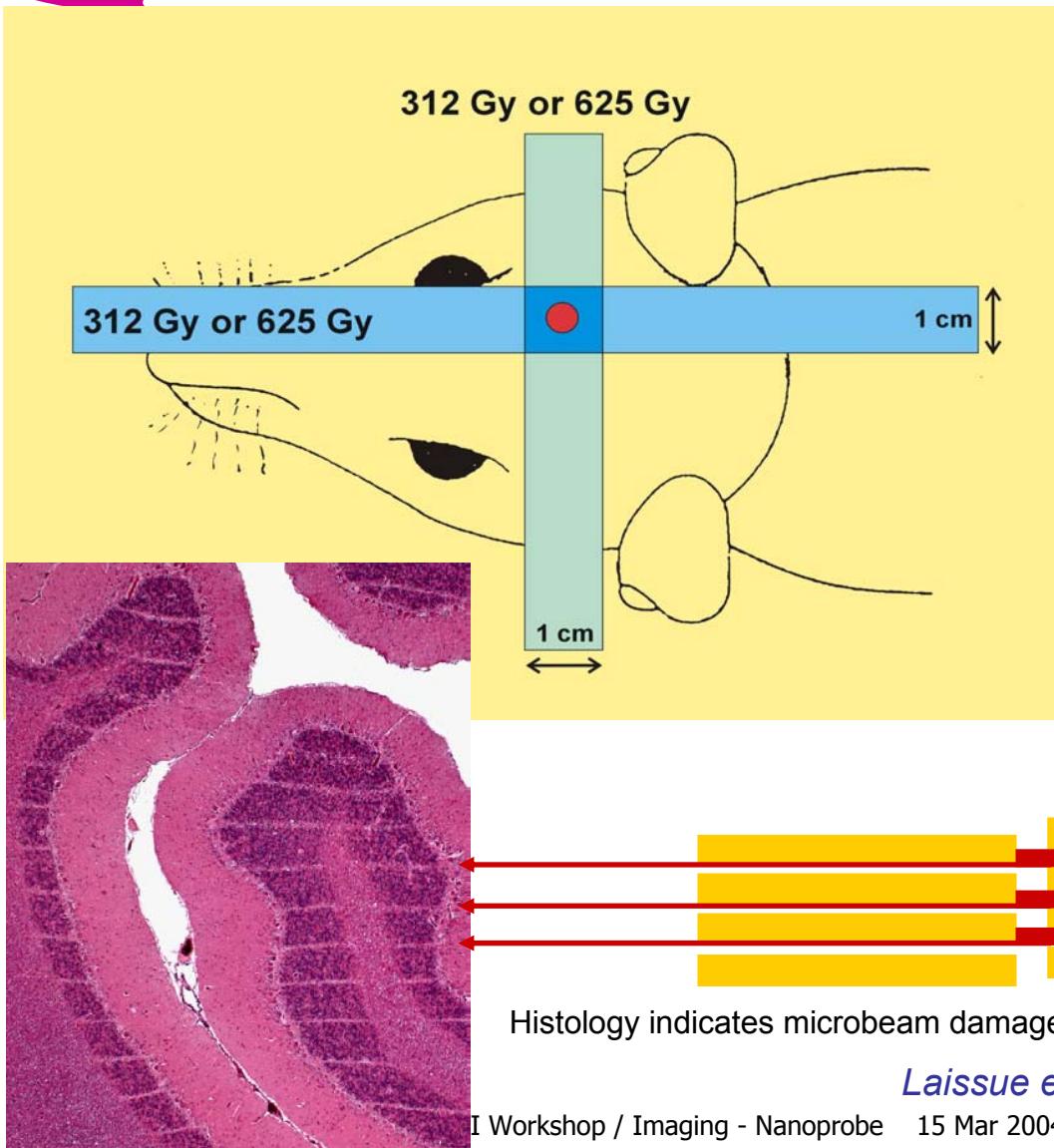


Microbeam Radiation Therapy

Mouse Brain, Visual Cortex



MRT of Rat Intracerebral Gliosarcomas



Fisher-344 rats bearing right frontal intecerebral 9L gliosarcomas ~4mm diameter
Treated 14 days after initiation

Synchrotron Radiation-

many opportunities for imaging and therapy

- ❖ Intense, wide energy range, small source size, polarized, pulsed
 - ❖ Small source
 - ❖ High spatial resolution
 - ❖ Coherence
 - ❖ Broadbanded radiation
 - ❖ Many absorption edges (~S to U)
 - ❖ X-ray absorption spectroscopy
 - ❖ Fluorescence XAS
 - ❖ Fluorescence Imaging
 - ❖ Dual energy imaging
 - ❖ Phase Contrast and DEI
 - ❖ Optimal imaging energies
 - ❖ Dose minimization for imaging
 - ❖ Dose optimization for therapy



Summary of Techniques

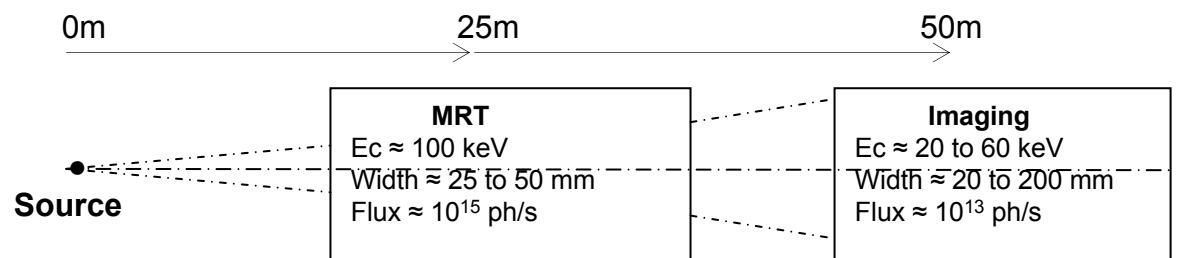
Technique	Beam Width	Resolution	Energy Range
KES – wide	200 mm	300 μm	20 – 60 keV
– narrow	20 mm	50 μm	20 – 60 keV
DEI – wide	150 mm	50 μm	20 – 90 keV
– narrow	15 mm	10 μm	20 – 90 keV
CT – wide	150 mm	50 μm	20 – 90 keV
– narrow	15 mm	10 μm	20 – 90 keV
CT Therapy	Uses the KES configuration and specification		20 – 60 keV
MRT	Needs high flux, high energy, minimal vibration amplitude and accurate positioning (5 μm peak-to-peak).		80 – 120 keV
Summary of techniques with required beam size, resolution, and spectral range required of the source. The sensitivity requirement for all techniques (both contrast agent and refraction density contrast) is approximately 1mg/cm ³ .			



Source Specifications for CLS

Need a superconducting wiggler

- High energies
- High flux
- Wide beam



Rough schematic layout beamline showing the relative location of the MRT and Imaging facilities along with horizontal beam widths and flux requirements.



Future

❖ New applications

❖ New methods

- ❖ Combination of existing methods – i.e. DEI and diffraction tomography?

- ❖ Microbeam imaging?

but...

❖ Must be driven by medical community!

- ❖ Significant effort into building a user group

- ❖ Workshops, seminars, pilot experiments, MD resident programs, etc.



*thank you for your
attention*



*Canadian Centre canadien
Light de rayonnement
Source synchrotron*



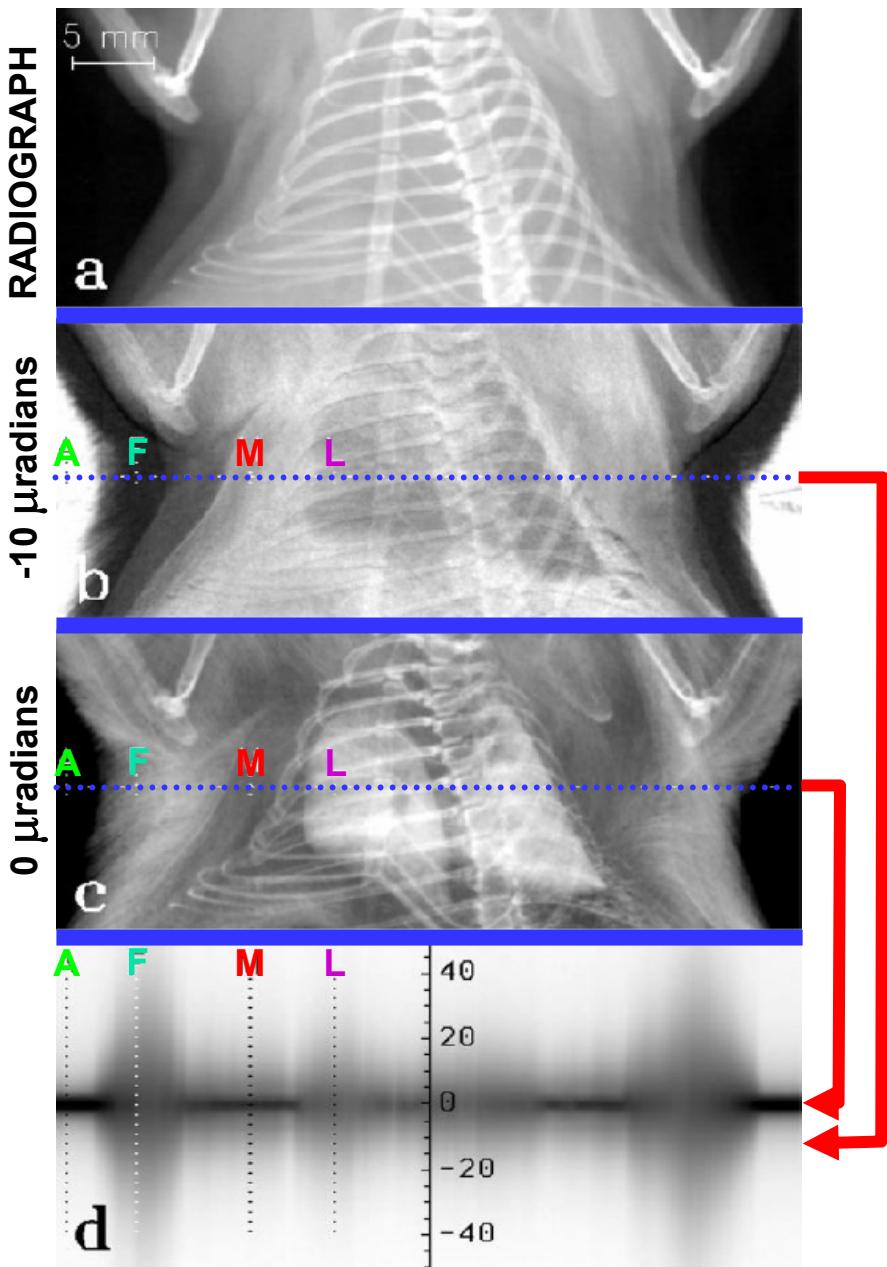
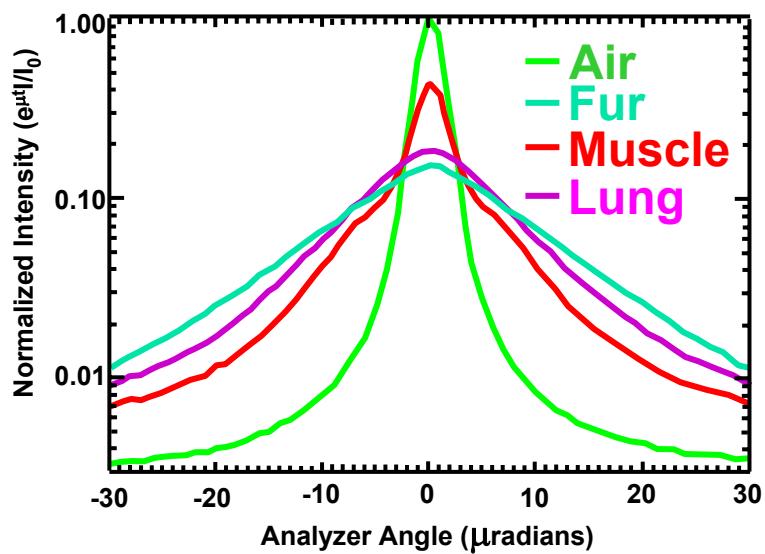
Other types of x-ray contrast?

- ✿ Key may be in anti-scatter considerations...
i.e. UP TO 90% OF X-RAYS IN SOME DIAGNOSTIC
IMAGING APPLICATIONS MAY BE OF SCATTER
ORIGIN!!
- ✿ Maybe we are looking at the wrong x-rays?
Can we use these scattered x-rays?
Not a new idea – i.e. X-ray Coherent Scatter Computed
Tomography (CSCT)
- ✿ But combining DEI with CSCT may bring a new
perspective to some medical imaging problems

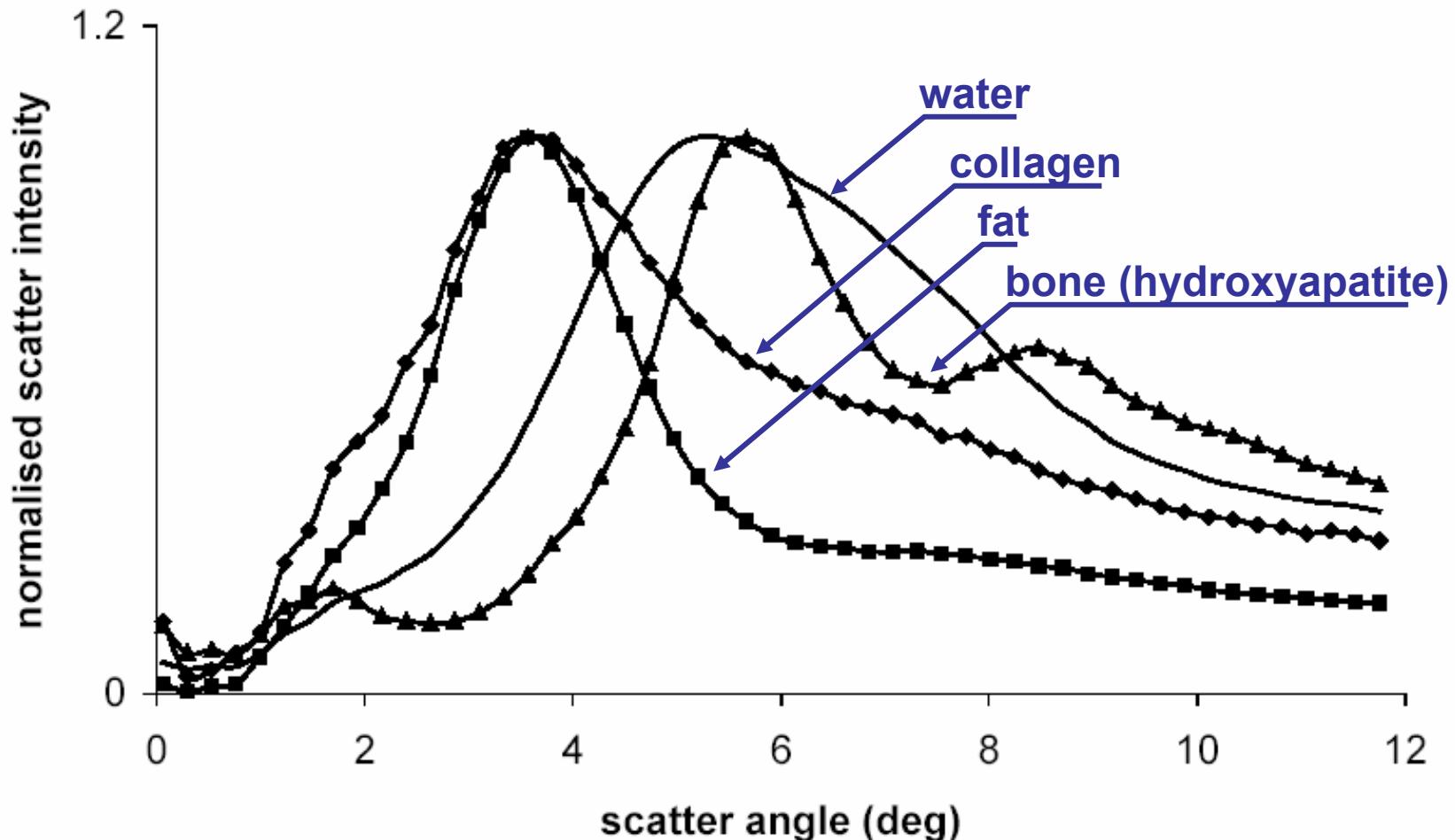


Rocking Curve Dependence

Rodent thorax
region at 18keV

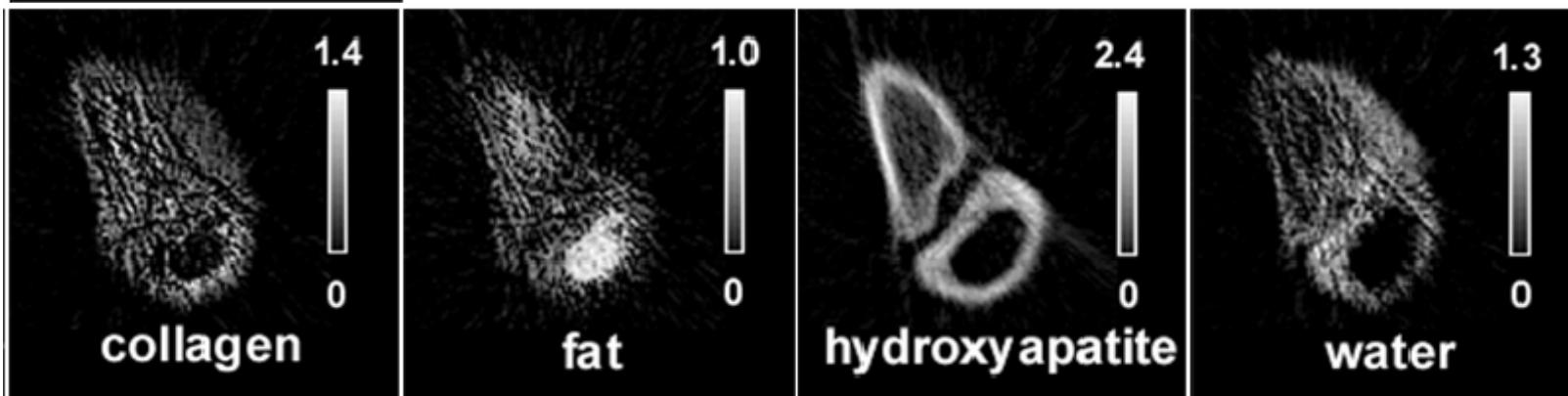
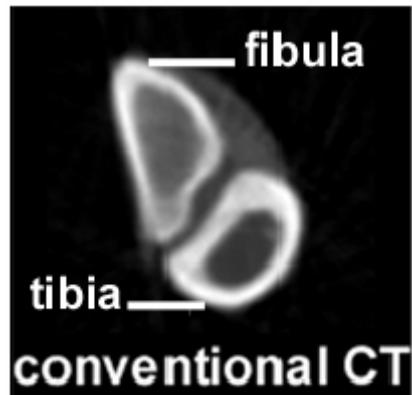


Scattering properties of some biological materials



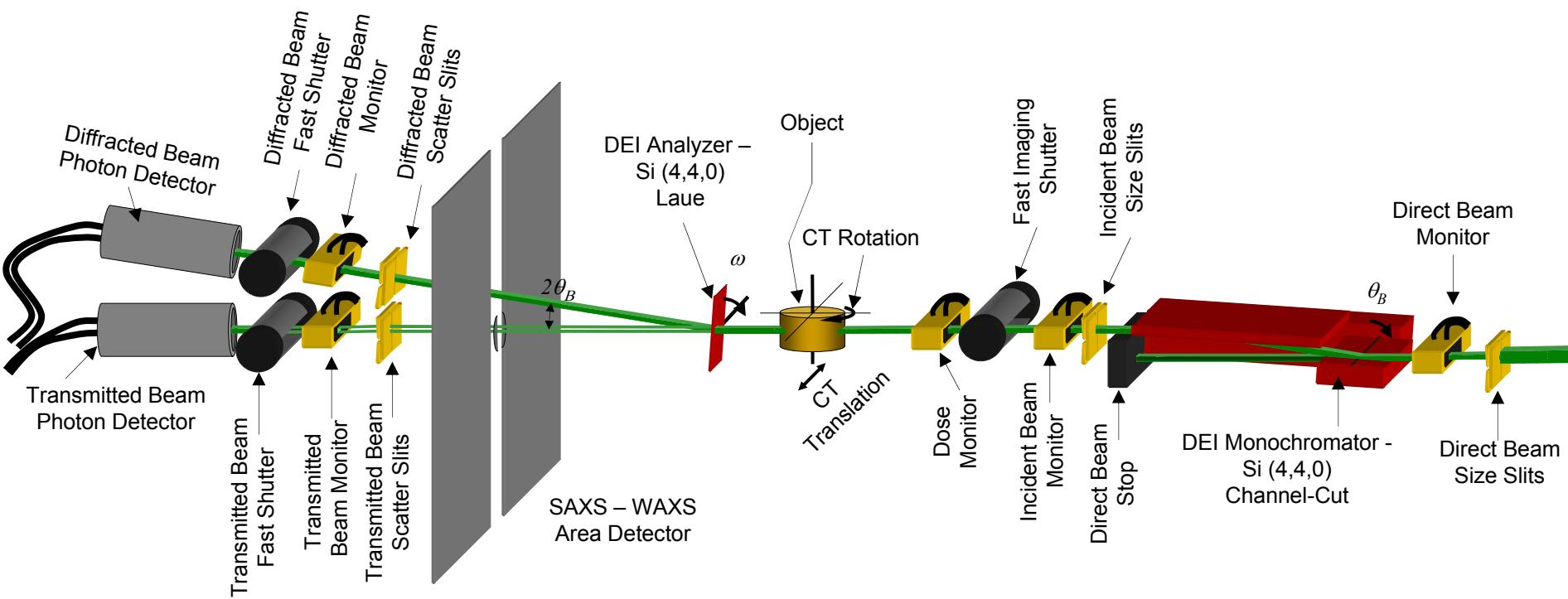
The momentum transfer range is $0 - 0.3 \text{ \AA}^{-1}$. ($0-3 \text{ nm}^{-1}$).
Information and figure courtesy Dr. Ian Cunningham.

Material Specific CT Imaging based on scattering properties

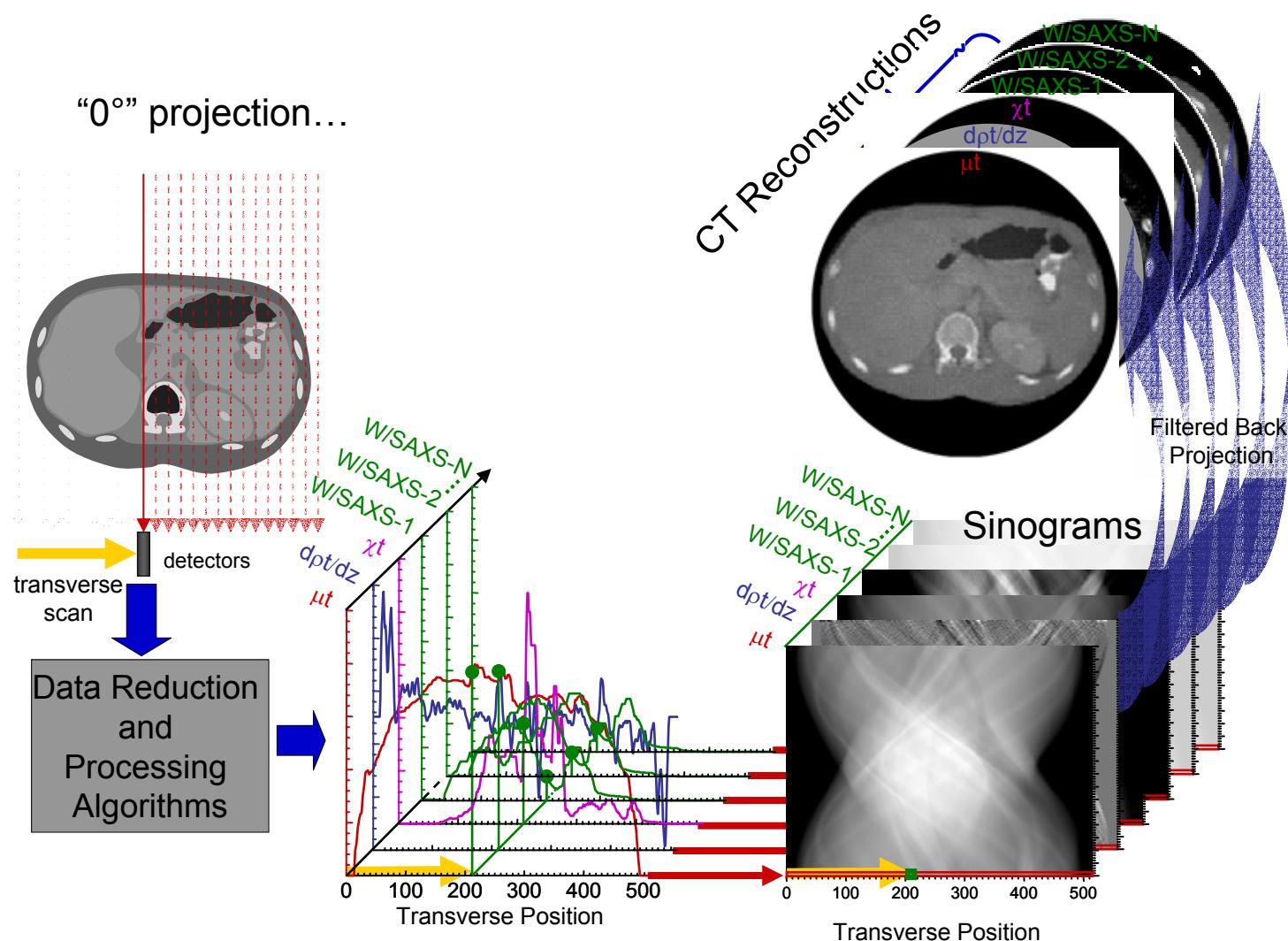


Information and figure courtesy Dr. Ian Cunningham.

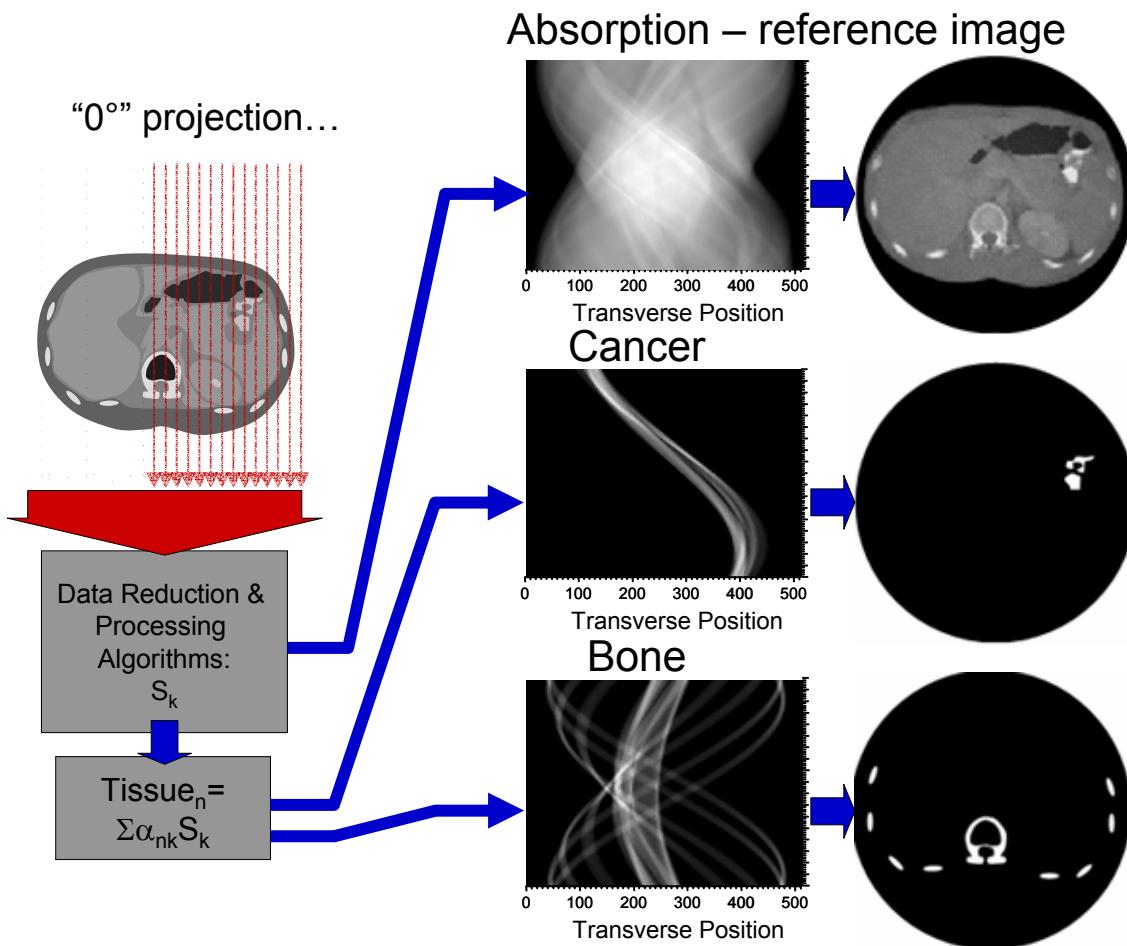
Combined Imaging System



Reconstruction Method



Tissue Identification



Conclusion

Many sources of contrast available –

- ❖ Absorption
- ❖ Density or refraction
- ❖ Scattering
 - ❖ Ultra-small angle scattering – sub-pixel features such as lung aveoli, hair, bone trabeculae...
 - ❖ Small angle scattering – large scale molecular arrangement such as collagen bundles, muscle fibers...
 - ❖ Wide angle scattering – atomic and molecular arrangement such as atomic and molecular nearest neighbor scattering...
- ❖ Fluorescence
- ❖ Compton



